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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/655,345	MCDANIEL, C. STEVEN	
	Examiner	Art Unit	
	SHERIDAN SWOPE	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 9.28 & 10.22.2009, and 1.8.2010.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) See Continuation Sheet is/are pending in the application.

4a) Of the above claim(s) See Continuation Sheet is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) See Continuation Sheet is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. _____ .
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)	5) <input type="checkbox"/> Notice of Informal Patent Application
Paper No(s)/Mail Date <u>0709;1009;0110.</u>	6) <input type="checkbox"/> Other: _____ .

Continuation of Disposition of Claims: Claims pending in the application are 1,15-28,31-35,37-52,55-63,67,69-75,79-108,110-256,272,309,319-362,365-373 and 376-394.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 28,31-35,37-52,55-63,90-93,101,103-108,120,136-179,183-216,218,243-250,256,322,325,328-342,357-359 and 386-388.

Continuation of Disposition of Claims: Claims rejected are 1,15-27,67,69-75,79-89,94-100,102,110-119,121-135,180-182,217,219-242,251-255,272,309,319-321,323,324,326,327,343-356,360-362,365-373,376-385 and 389-394.

DETAILED ACTION

Applicant's filings of September 28 and October 22, 2009, and January 8, 2010, in response to the action of March 27, 2009, are acknowledged.

The currently elected invention is directed to an aqueous paint comprising an organophosphorus hydrolase that is a *Flavobacterium* sp opd gene product comprising a Co²⁺ ion, wherein the paint comprises a thermoplastic binder, a filler and a bactericide preservative, and the paint forms a film under ambient conditions, and wherein the paint does not have additional inorganic compounds, organic compounds, or a plasticizer.

Based on Applicant's filings, Claims 2-14, 29, 30, 36, 53, 54, 64-66, 68, 76-78, 109, 257-271, 273-308, 310-318, 363, 364, 374, and 375 stand cancelled, Claims 1, 119, 122, 272, 309, 319, 320, and 368 are amended, and Claims 393 and 394 are added. Claims 1, 15-28, 31-35, 37-52, 55-63, 67, 69-75, 79-108, 110-256, 272, 309, 319-362, 365-373, and 376-394 are pending. Claims 28, 31-35, 37-52, 55-63, 90-93, 101, 103-108, 120, 136-179, 183-216, 218, 243-250, 256, 322, 325, 328-342, 357-359, and 386-388 were previously withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions. Claims 1, 15-27, 67, 69-75, 79-89, 94-100, 102, 110-119, 121-135, 180-182, 217, 219-242, 251-255, 272, 309, 319-321, 323, 324, 326, 327, 343-356, 360-362, 365-373, 376-385, and 389-394 are hereby examined.

Priority

The priority date for the currently examined claims is September 9, 2002.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Claims 1, 15-27, 67, 69-75, 79-89, 94-100, 102, 110-119, 121-135, 180-182, 217, 219-242, 251-255, 272, 309, 319-321, 323, 324, 326, 327, 343-356, 360-362, 365-373, 376-385, and 389-394 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-109 of US Application 12/474,921. Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 1, 15-27, 67, 69-75, 79-89, 94-100, 102, 110-119, 121-135, 180-182, 217, 219-242, 251-255, 272, 309, 319-321, 323, 324, 326, 327, 343-356, 360-362, 365-373, 376-385, and 389-394 herein and Claims 1-109 of 12/474,921 are both directed to a coating/paint comprising an enzyme of E.C. 3.1.8. The claims differ in that Claims 1-109 of 12/474,921 are not limited to enzymes of E. C. 3.1.8, while Claims 1, 15-27, 67, 69-75, 79-89, 94-100, 102, 110-119, 121-135, 180-182, 217, 219-242, 251-255, 272, 309, 319-321, 323, 324, 326, 327, 343-356, 360-362, 365-373, 376-385, and 389-394 are limited to enzymes of E. C. 3.1.8. The portion of the specification in 12/474,921 that supports the recited coatings includes embodiments that would anticipate Claims

1, 15-27, 67, 69-75, 79-89, 94-100, 102, 110-119, 121-135, 180-182, 217, 219-242, 251-255, 272, 309, 319-321, 323, 324, 326, 327, 343-356, 360-362, 365-373, 376-385, and 389-394 herein, e.g., a coating/paint comprising an enzyme of E.C. 3.1.8, which are also coatings recited in Claims 1-109 of 12/474,921. Claims 1, 15-27, 67, 69-75, 79-89, 94-100, 102, 110-119, 121-135, 180-182, 217, 219-242, 251-255, 272, 309, 319-321, 323, 324, 326, 327, 343-356, 360-362, 365-373, 376-385, and 389-394 herein cannot be considered patentably distinct over Claims 1-109 of 12/474,921 when there are specifically recited embodiments (a coating/paint comprising an enzyme of E.C. 3.1.8) that would anticipate Claims 1, 15-27, 67, 69-75, 79-89, 94-100, 102, 110-119, 121-135, 180-182, 217, 219-242, 251-255, 272, 309, 319-321, 323, 324, 326, 327, 343-356, 360-362, 365-373, 376-385, and 389-394 herein. Alternatively, Claims 1, 15-27, 67, 69-75, 79-89, 94-100, 102, 110-119, 121-135, 180-182, 217, 219-242, 251-255, 272, 309, 319-321, 323, 324, 326, 327, 343-356, 360-362, 365-373, 376-385, and 389-394 herein cannot be considered patentably distinct over Claims 1-109 of 12/474,921 when there are specifically disclosed embodiments in 12/474,921 that supports Claims 1-109 of that application and falls within the scope of Claims 1, 15-27, 67, 69-75, 79-89, 94-100, 102, 110-119, 121-135, 180-182, 217, 219-242, 251-255, 272, 309, 319-321, 323, 324, 326, 327, 343-356, 360-362, 365-373, 376-385, and 389-394 herein, because it would have been obvious to a skilled artisan to modify the coatings of Claims 1-109 of 12/474,921 by selecting specifically disclosed embodiments that supports those claims, i.e., a coating/paint comprising an enzyme of E.C. 3.1.8, as disclosed in 12/474,921. One having ordinary skill in the art would have been motivated to do this, because such an embodiment, a coating/paint comprising an enzyme of E.C. 3.1.8, is disclosed as being a preferred embodiment within Claims 1-109 of the other application. This is a provisional

obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the following reasons.

For Claims 21-27, the phrases "functional equivalent", "structural analog", and "sequence analog" render the claims indefinite. The specification states:

[0121] ...As used herein, a "functional equivalent" to the wild-type enzyme is a proteinaceous molecule comprising a sequence and/or a structural analog of a wild-type enzyme's sequence and/or structure and functions as an enzyme. The functional equivalent enzyme may possess similar or the same enzymatic properties, such as catalyzing chemical reactions of the wild-type enzyme's EC classification, or may possess other desired enzymatic properties, such as catalyzing the desirable chemical reactions of an enzyme that is related to the wild-type enzyme by sequence and/or structure. Examples of a functional equivalent of a wild-type enzyme are described herein, and include mutations to a wild-type enzyme sequence, such as a sequence truncation, an amino acid substitution, an amino acid modification, a fusion protein, or a combination thereof, wherein the altered sequence functions as an enzyme.

[0169] It is particularly contemplated that a functional equivalent enzyme comprising a structural analog and/or sequence analog may possess an enhanced desirable property and/or a reduced undesirable property, in comparison to the enzyme upon which it is based. ...As used herein, a "structural analog" refers to one or more chemical modifications to the peptide backbone or non-side chain chemical moieties of a proteinaceous molecule. In certain aspects, a subcomponent of an enzyme such as an apo-enzyme, a prosthetic group, a co-factor, or a combination thereof, may be modified to produce a functional equivalent structural analog. In particular facets, such an enzyme sub-component that does not comprise a proteinaceous molecule may be altered to produce a functional equivalent structural analog of an enzyme when combined with the other sub-components. As used herein, a "sequence analog" refers to one or more chemical modifications to the side chain chemical moieties, also known herein as a "residue" of one or more amino acids that define a proteinaceous molecule's sequence. Often such a "sequence analog" comprises an amino acid substitution, which is generally produced by recombinant expression of a nucleic acid comprising a genetic mutation to produce a mutation in the expressed amino acid sequence.

Said statements do not define the phrases “functional equivalent”, “structural analog”, and “sequence analog” because (i) disclosure of what activity the encompassed enzymes may possess is not disclosure of what activity the encompassed enzymes do possess, (ii) examples are not definitive, (iii) the “desirable chemical reactions”, “other desired enzymatic properties”, “desirable property”, and “undesirable property” are not defined, (iv) the terms “similar” and “such as” are indefinite. Thus, based on said statements, the structural and functional limitations of the genera of any “functional equivalent”, “structural analog”, or “sequence analog” is unclear. The skilled artisan would not know the metes and bounds of the recited invention.

Any subsequent rejection based, on clarification of the above phrases and terms, will not be considered a new ground for rejection.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Rejection of Claims 1, 15-27, 67, 69-75, 79-89, 94-100, 102, 110-119, 121-135, 180-182, 217, 219-242, 251-255, 272, 309, 319-321, 323, 324, 326, 327, 343-356, 360-362, 365-373, 376-385, and 389-392 under 35 U.S.C. 112, first paragraph/enablement, for some of the reasons explained in the prior actions is maintained. Claims 393 and 394 are herein rejected under 35 U.S.C. 112, first paragraph/enablement for the same reasons. Upon reconsideration, the reasons set forth below are used for the rejection of the claims under 35 U.S.C. 112, first paragraph/enablement. The reasons set forth below were included in the prior reasons for the instant rejection. However, some reasons previously used for the rejection of claims under 35

U.S.C. 112, first paragraph/ enablement, are no longer deemed to be valid; thus, it is acknowledged that enzymes of E.C. 3.1.8 as well as methods for making and using paints are known in the art. However, methods for making and using paints comprising active enzymes of E.C. 3.1.8 were not known in the art nor are they enabled by the specification for the reasons explained below.

Claims 1, 15-27, 67, 69-75, 79-89, 94-100, 102, 110-119, 121-135, 180-182, 217, 219-242, 251-255, 272, 309, 319-321, 323, 324, 326, 327, 343-356, 360-362, 365-373, 376-385, and 389-394 are rejected under 35 U.S.C. 112, first paragraph/enablement, for the following reasons. The prior art is enabling for the paints anticipated by Bonaventura et al, 1999 and paints rendered obvious by Bonaventura et al in view of (i) Di Sioudi et al, 1999 and ExPASy E.C.3.1.8, (ii) Pieczenik et al, 1993, (iii) Sigma, Inc, (iv)Pusch et al, 1985, (v) Miller et al, 2005, (vi)Ye et al, 1999, (vii) Krumhar et al, 1992, or (viii)Yafuso et al, 1991 (see below for rejections under 35 USC 102(b) and 103(a)). However, the specification does not reasonably provide enablement for any type of paint, comprising any components, and comprising any active enzyme of E.C. 3.1.8. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In regards to this enablement rejection, the application disclosure and claims are compared per the factors indicated in the decision In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). These factors are considered when determining whether there is sufficient evidence to support a description that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. The factors include but are not limited to: (1) the nature of the invention; (2) the breadth of the claims; (3) the predictability or

unpredictability of the art; (4) the amount of direction or guidance presented; (5) the presence or absence of working examples; (6) the quantity of experimentation necessary; (7) the relative skill of those skilled in the art. Each factor is here addressed on the basis of a comparison of the disclosure, the claims, and the state of the prior art in the assessment of undue experimentation.

Claims 1, 15-27, 67, 69-75, 79-89, 94-100, 102, 110-119, 121-135, 180-182, 217, 219-242, 251-255, 272, 309, 319-321, 323, 324, 326, 327, 343-356, 360-362, 365-373, 376-385, and 389-394 are so broad as to encompass any type of paint, comprising any components, and comprising any active enzyme of E.C. 3.1.8. The scope of each of these claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of paints comprising an active enzyme of E.C. 3.1.8, or variant or analog thereof, as broadly encompassed by the claim. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity in paint, comprising any components, requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. However, in this case the enablement is limited to the paints anticipated by Bonaventura et al, 1999 and paints rendered obvious by Bonaventura et al in view of (i) Di Sioudi et al, 1999 and ExPASy E.C.3.1.8, (ii) Piesecki et al, 1993, (iii) Sigma, Inc, (iv) Pusch et al, 1985, (v) Miller et al, 2005, (vi) Ye et al, 1999, (vii) Krumhar et al, 1992, or (viii) Yafuso et al, 1991.

It is acknowledged that enzymes of E.C. 3.1.8 as well as methods for making and using paints are known in the art. However, methods for making and using paints comprising active

enzymes of E.C. 3.1.8 are not known in the art. While recombinant and mutagenesis techniques as well as methods for testing the activity of E.C. 3.1.8 enzymes are known, it is not routine in the art to screen an essentially unlimited number of proteins, and variants and analogs thereof, for activity within any paint comprising any components, as encompassed by the instant claims. Furthermore, the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the results of such modifications are unpredictable (Galye et al, 1993; Whisstock et al, 2003). In addition, one skilled in the art would expect any tolerance to modification of any given protein having the desired biological characteristics to diminish with each further and additional modification.

The specification does not support the broad scope of Claims 1, 15-27, 67, 69-75, 79-89, 94-100, 102, 110-119, 121-135, 180-182, 217, 219-242, 251-255, 272, 309, 319-321, 323, 324, 326, 327, 343-356, 360-362, 365-373, 376-385, and 389-394, which encompasses all paints, comprising any components, and comprising any active enzyme of E.C. 3.1.8. The specification does not support the broad scope of said claims because the specification does not establish: (A) the structure of any enzyme of E.C. 3.1.8, or variants or analogs thereof, that are active within any paint, comprising any components, (B) regions of any enzyme having the desired biological characteristics that may, or may not, be modified without affecting the activity within any paint; (C) the general tolerance of any E.C. 3.1.8 enzyme, having activity within any paint, to modification and extent of such tolerance; (D) a rational and predictable scheme for identifying or making the genus of E.C. 3.1.8 enzymes having activity within any paint; (E) the compositions of paints that allow enzymes of E.C. 3.1.8 to be active; (F) the compositions of paints that inhibit the activity of E.C. 3.1.8 enzymes; (G) components of any paint that may, or

may not, be modified without affecting the activity of any E.C. 3.1.8 enzyme; (H) a rational and predictable scheme for identifying components of paints having the desired property of allowing any E.C. 3.1.8 enzyme to be active; (I) the identity of any paints wherein the comprised enzyme of E.C. 3.1.8 is stable for more than one month or more than one year; and (J) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of paints comprising any active E.C. 3.1.8 enzyme or analog thereof. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of paints having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In support of their request that the prior rejections under 35 USC 103(a) be withdrawn, Applicants provide the following arguments, which are relevant to the rejections above. These arguments are not found to be persuasive for the reasons following each argument.

(A) The Examiner acknowledged (pgs 4 & 6) enablement of the organophosphorous hydrolase as described in Examples 3-5 and the fillers as described in Example 14.

(A) Reply: It is noted that the specification fails to disclose the structure/sequence of the organophosphorus hydrolase used in Examples 3-5. Thus, the specification fails to enable the skilled artisan to make and use the paint disclosed therein. Nonetheless, the prior art enables

the skilled artisan to make and use the paints anticipated by Bonaventura et al, 1999 and paints rendered obvious by Bonaventura et al in view of (i) Di Sioudi et al, 1999 and ExPASy E.C.3.1.8, (ii) Pielecki et al, 1993, (iii) Sigma, Inc, (iv) Pusch et al, 1985, (v) Miller et al, 2005, (vi) Ye et al, 1999, (vii) Krumhar et al, 1992, or (viii) Yafuso et al, 1991.

(B) The Examiner previously stated (action of May 18, 2007, parg brd pg 6-7):

“The specification may be enabling for a broader scope of coatings than just a paint comprising enzymatically active organophospho-hydrolase. However, for the reasons stated in the prior action and in (A) above, the specification if not enabling for the full scope of the recited invention.”

In light of this broader enablement of coatings and enzymes other than a paint comprising an organophospho-hydrolase, Applicant finds the current rejection an inappropriate and unsupportable reversal regarding the enablement of the specification, particularly in regards to points (E) to (Q) in the current Office Action as they relate to coatings and paints.

(B) Reply: It is noted that the statement in the action of May 18, 2007 says that “The specification may be enabling for a broader scope of coatings than just a paint comprising enzymatically active organophospho-hydrolase. Said statement does not assert that the specification is enabling for a broader scope of coatings or which specific coatings the specification is enabling for.

It is acknowledged that the art is enabling for many types of coatings per se. However, neither the specification nor the prior art is enabling for which enzymes, having which structures and activities, retain their activity(s) when in a composition that is a coating, such as paint comprising any components.

(C) How to make and use a coating such as a paint is a well-developed art, and the specification further provides ample direction and guidance to those of skill in the art on production a coating, as well as selection and incorporation of standard coating components such

as thermoplastic binders, fillers and bactericide preservatives, to produce a coating with the properties cited in points.

(C) Reply: It is acknowledged that, methods for making and using paints, is a well-developed art. However, methods for making and using paints comprising active enzymes, is not a well-developed art.

(D) The Examiner's reply to previous argument (B) that "the scope of the proteins...is even broader than the scope encompassed by any organophosphorus hydrolase" is refuted by Applicant, based on the past agreement by the Examiner of [broader scope ??] at the Office Action mailed May 18, 2007, and the disclosures of specification supporting such scope as described herein and in prior filed documents.

(D) Reply: The Examiner is not completely clear of what is being argued. The scope of the current claims encompasses any type of paint, comprising any components, and comprising any active enzyme of E.C. 3.1.8. Said enzymes are known as aryldialkylphosphatases/organophosphorus hydrolase, α -esterases, aryltriphosphatases, paraoxon hydrolases, paraoxonases, and phosphotriesterases, which act on organophosphorus compounds (such as paraoxon) including esters of phosphonic and phosphinic acids (ExPASY proteomics server/ENZYME/SIB).

(E) In regard to the quantity of experimentation necessary, the specification describes various assays for organophosphorous hydrolase activity at ¶¶ 0636-0646 that are routine in the art to conduct. In particular, Example 19 describes a simple assay for paroxonase activity using standard laboratory equipment.

(E) Reply: In the instant case, the scope of the claims encompasses any type of paint, comprising any components, and comprising any active enzyme of E.C. 3.1.8. As stated above,

methods for testing the activity of enzymes of E.C. 3.1.8 are known. However, testing any protein or analog, having any structure and the activity of any enzyme of E.C. 3.1.8, for activity in an unlimited number of paints, comprising any components, represents undue experimentation. It is acknowledged that a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.

Also, see (H), below.

(F) Part of the definition of enzyme activity EC 3.1.8 is the cleavage of one or more organophosphorous chemical species, often one or more species of organophosphorus chemical warfare agent(s) and/or pesticide(s).

(F) Reply: It is acknowledged that EC 3.1.8 enzymes cleave one or more organophosphorous chemical species. However, the specification fails to teach which organophosphorous chemical species are cleaved by which EC 3.1.8 enzymes in which paints comprising which components.

(G) The specification has cited numerous specific residues that may be modified, for embodiments wherein site directed alterations are desired (see, for example, ¶¶ 0154-0191 and 0194-0240 regarding altering structure of proteins).

(G) Reply: It is acknowledged that the specification at ¶¶ 0184-0191 describes residues of the OPH of Benning et al that are important for hydrolase activity. However, said paragraphs do not disclose residues of said OPH, or any other E.C. 3.1.8 enzyme, that are important for hydrolase activity within any paint, comprising any components.

(H) The Examiner's position that one must have knowledge and guidance of an amino acid that may be altered is incorrect, as an enzyme may be modified and hundreds or thousands

of possible variants assayed without such knowledge and guidance of the specific residues that are altered, and in fact, such techniques are used to identify the specific residues that contribute to activity. Or in other words, alterations may be readily made, including, for example evolutionary selection as described at ¶ 0181 and/or chemical modifications described at ¶¶ 0159 and 0160, and assays used to readily identify active variants, followed by determination of specific residues that influence activity. Techniques for such alterations and assays are described in the specification. The amount of experimentation is routine given the techniques and assays that are used.

(H) Reply: It is acknowledged that an enzyme may be modified and, with some assays, hundreds or thousands of possible variants assayed without knowledge of the specific residues that are altered. However, without guidance, the public is left to trial and error making and testing of the essentially unlimited possible combinations of E.C. 3.1.8 enzymes and paints comprising any components.

Guo et al, 2004 teaches that the percentage of random single-substitution mutations, which inactivate a protein, using a protein 3-methyladenine DNA glycosylase as a model, is 34% and that this number is consistent with other studies in other proteins (pg 9206, parg 4). Guo et al further show that the percentage of active mutants for multiple mutations appears to be exponentially related to this by the simple formula $(0.66)^X \times 100\%$ where X is the number of mutations introduced (Table 1). Assuming that the *Flavobacterium* organophosphorus hydrolase of Bonaventura et al is the same as, or similar to, GenBank AY766084, with 365 amino acids, the following calculation can be made. Applying the estimate of Guo et al, 80% identity to the hydrolase of Bonaventura et al allows up to 73 mutations within said 365 amino acids and, thus, only $(0.66)^{73} \times 100\%$ or $6.7 \times 10^{-12}\%$ (one out of 1.5×10^{11}) of random mutants having 80%

identity would be active. Moreover, the instant claims fail to provide any structural limitations, thus an even smaller percentage of proteins would be expected to have the desired activity. Current techniques in the art (i.e., high throughput mutagenesis and screening techniques) would allow for finding a few active mutants within several hundred thousand or up to about a million inactive mutants, despite even this being an enormous quantity of experimentation that would take a very long time to accomplish. But finding a few mutants within several billion or more, as in the genus of proteins having 80% identity or less, would not be possible. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance includes directing the skilled artisan to which residues, motifs, and domains of any E.C. 3.1.8 enzyme that may, or may not, be altered and still retain E.C. 3.1.8 enzyme activity within any paint comprising any components.

(I) The Examiner has not met the burden to show that the claims are not adequately described or lack of enablement due to a "lack of specific sequence."

In Capon v. Eshhar, 418 F.3d at 1349, 1358, 76 USPQ2d at 1084, the Federal Circuit held that the Board of Patent Appeals and Interferences (BPAI):

"erred in ruling that § 112 imposes a per se rule requiring recitation in the specification of the nucleotide sequence of the claimed DNA, when that sequence is already known in the field, at 1349

The Board erred in holding that the specifications do not meet the written description requirement because they do not reiterate the structure or formula or chemical name for the nucleotide sequences of the claimed chimeric genes, at 1358"

In Invitrogen Corp. v. Clontech Laboratories, Inc., 429 F.3d 1052, 1073 (Fed. Cir. 2005) the court upheld a district court decision that claims to a polypeptide encoded by a modified

reverse transcriptase nucleotide sequence were not invalid under the written description requirement, even though the claims were not limited to sequences recited in the specification.

(I) Reply: It is acknowledged that what is known in the art need not be taught for the specification to be enabling or descriptive. It is acknowledged that the specification need not teach every species for a genus to be enabled. However, the specification fails to enable the instant claims because the specification fails to disclose the structure/sequence of any E.C. 3.1.8 enzyme that is active within any paint. While the prior art teaches that the enzyme of Bonaventura et al is useful in a paint (see rejections below), said teachings do not enable the skilled artisan to make and use any paint, comprising any components, and comprising an active enzyme of any E.C. 3.1.8.

(J) Applicants have also included a copy of the Materials Data Sheet ("MDS") of the paint used in Example 3-5 as Exhibit A for reference to the binder(s), filler(s) and biocide preservative(s) that are described as components of this paint. Note that a specific biocide preservative is not listed, and Applicant understands that it is common practice not to list various minor components (e.g., additives such as a preservative) in a coating's MDS.

(J) Reply: It is acknowledged that Applicants have provided a copy of the MDS of the paint used in Example 3-5. However, neither said MDS nor the specification provides the structure/sequence of an E.C. 3.1.8 enzyme used in said examples.

Written Description

Rejection of Claims 1, 15-27, 67, 69-75, 79-89, 94-100, 102, 110-119, 121-135, 180-182, 217, 219-242, 251-255, 272, 309, 319-321, 323, 324, 326, 327, 343-356, 360-362, 365-373, 376-385, and 389-392 under 35 U.S.C. 112, first paragraph/written description, for some of the reasons explained in the prior actions is maintained. Claims 393 and 394 are herein rejected

under 35 U.S.C. 112, first paragraph/enablement for the same reasons. Upon reconsideration, the reasons set forth below are used for the rejection of the claims under 35 U.S.C. 112, first paragraph/written description. The reasons set forth below were included in the prior reasons for the instant rejection. However, some reasons previously used for the rejection of claims under 35 U.S.C. 112, first paragraph/written description, are no longer deemed to be valid; thus, it is acknowledged that enzymes of E.C. 3.1.8 as well as methods for making and using paints are known in the art. However, methods for making and using paints comprising active enzymes of E.C. 3.1.8 were not known in the art nor are they sufficiently described by the specification for the reasons explained below.

Claims 1, 15-27, 67, 69-75, 79-89, 94-100, 102, 110-119, 121-135, 180-182, 217, 219-242, 251-255, 272, 309, 319-321, 323, 324, 326, 327, 343-356, 360-362, 365-373, 376-385, and 389-392 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of paints, comprising any components, and comprising any enzyme of E.C. 3.1.8, wherein the enzyme is active within said paint. While the specification describes one species of such paints, such that the skilled artisan would believe, applicants were in possession at the time of filing, the specification fails to describe the structure/sequence of the E.C. 3.1.8 enzyme within the paint. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of being a paint, comprising any components, and comprising any enzyme of E.C. 3.1.8, wherein the enzyme is active within the paint. In addition, the specification fails to describe any paint, wherein the enzyme is active within the paint for greater than one month or

greater than one year. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

In support of their request that said rejection be withdrawn, Applicants provide the some of the same arguments presented above for the rejection under 35 USC 112 first paragraph/enablement. These arguments are not found to be persuasive for the reasons explained above.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 15-20, 67, 69-72, 74, 75, 79-89, 94-100, 102, 110-119, 121-135, 180-182, 217, 219-223, 234-238, 251-255, 272, 319, 320, 343, 344, 351-352, 354-356, 360-362, 365-373, 376-385, 389-394 are rejected under 35 U.S.C. 102(b) as being anticipated by Bonaventura et al, 1999, as evidenced by W. R. Grace & Co. Bonaventura et al teaches latex and oil-based paints comprising an isolated active E.C. 3.1.8 Flavobacterium enzyme that cleaves parathion (Example V), i.e., an aryldialkylphosphatase/organophosphorus hydrolase of E.C. 3.1.8.1. The paints of Bonaventura et al comprise polyurethane hydrogel, which has a thermoplastic binder, silica microspheres, and an anti-foamer (Grace, Inc). The skilled artisan would believe that, more likely than not, the paints of Bonaventura et al comprise a pigment and have some chalking that is self-cleaning. The paints of Bonaventura et al are initially multi-pack, with the polyurethane in a separate pack from the water- or solvent-based coating. Therefore, Claims 1, 15-21, 67, 72, 74, 75, 79-89, 94-100, 102, 110-119, 121-135, 180-182, 217, 219-223, 234-238, 251-255, 272,

319, 320, 343, 344, 351-352, 354-356, 360-362, 365-373, 376-385, 389-394 are rejected under 35 U.S.C. 102(b) as being anticipated by Bonaventura et al, 1999, as evidenced by as evidenced by W. R. Grace & Co.

In support of their request that the prior rejection of Claims 1, 67, 69-75, 79, 80, 82, 83, 88, 89, 94-97, 110-112, 126-131, 180- 182, 217, 252, 319, 320, 323, 324, 343, 344, 351-354, 365, 368-370, 376, 380-385 and 391 under 35 U.S.C. 103(a), Applicants provide the following arguments, which are relevant to the rejection above. These arguments are not found to be persuasive for the reasons following each argument.

(A) Bonaventura does not teach, suggest or provide motivation to create a non-marine coating or paint, that is, Bonaventura does not teach, suggest or provide any motivation to create a composition for use other than one in contact with an aquatic environment for an antifouling purpose.

(A) Reply: The instant claims do not exclude paints for marine surfaces. Many of the surfaces recited in Claim 1 can be marine surfaces. Moreover, there was an expectation that the paint of Bonaventura can be used on surfaces other than marine surfaces.

(B) It would not be obvious to one skilled in the art to modify the paint described in Bonaventura, formulated for use in contact with an aqueous environment for an antifouling property, into another type of paint that is formulated to be suitable for a purpose of use in other environments, and with an accordingly reduced or lacking antifouling property.

(B) Reply: The claims do not recite a paint that is reduced in or lacking antifouling properties or that the encompassed paints must be better than the paint of Bonaventura for use in other environments. It is noted that the claims do encompass paints comprising a biocide, Which is an antifouling component.

(C) Ascertaining the differences between the prior art and the claims at issue requires interpreting the claim language, and considering both the invention and the prior art references as a whole (MPEP 2141.02). Applicant finds that Bonaventura as a whole is directed to materials suitable for a marine/aquatic environment that incorporate antifouling agents for a purpose of protecting surfaces that contact aquatic, fouling environments. As described at M.P.E.P. 2143.01 R-6] V:

If proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984)

(C) Reply: There is no evidence that the paint of Bonaventura et al would be unsatisfactory for the surfaces recited in the instant claims.

(D) The present claims are non-obvious over Bonaventura, as there is no reasonable expectation of success for prolonged use of a hydrolytic enzyme, which uses a water molecule to catalyze cleavage of a chemical bond, in a material not hydrated by contact with an aqueous medium. A freeze dried hydrolytic enzyme is non-functional, and an inhibition of function would also be expected in a coating not continuously or near continuously hydrated by contact with an aqueous medium.

(D) Reply: (i) The claims do not recite that the enzyme is not hydrated by contact with an aqueous medium. The claims recite “a paint” not “a dehydrated paint”. (ii) The skilled artisan would believe that, more likely than not, environmental humidity would provide sufficient water to support some hydrolase activity. In support of said belief, other enzymes were known to be active in as low as 20% humidity (Won et al, 2001, Fig 5a; Yang et al, 1996, Fig 2a). (iii) Neither Bonaventura et al nor the instant claims a freeze dried hydrolytic enzyme.

(E) Bonaventura does not teach, suggest or provide motivation to create a surface treatment or a coating with an enzymatically active organophosphorus hydrolase which is capable of exhibiting catalyzing activity in the surface treatment at one or more instances after the surface treatment has been formed with the enzymatically active organophosphorus hydrolase for greater than approximately 1 week (Claims 319 and 368).

(E) Reply: Bonaventura teaches that the parathion-cleaving enzyme is active within a dried coating after five days; including, four days of drying and one day of testing (Example V; Table I). Therefore, the skilled artisan would believe that, more likely than not, the enzyme is active after one week. Since the Office does not have the facilities for examining and comparing applicants' paint with the paint of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the parathion-cleaving enzyme of the prior art does not possess the same material structural and functional characteristics of the claimed protein, including activity in the paint for greater than one month or greater than one year). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

(F) Applicant, while reviewing Bonaventura, found mention of a hydrolytic enzyme that cleaves parathion in a mixture of a hydrophilic polyurethane and a paint, at Example V, column 34 line 35 - column 35, line 27.

(F) Reply: It is unclear whether Applicants have put forward the above statement as an argument. Nonetheless, the Examiner makes the following comments. It is assumed that Applicants are asserting that Bonaventura et al does not teach a paint comprising a hydrolytic enzyme that cleaves parathion because the composition of Bonaventura et al is a mixture of a hydrophilic polyurethane and a paint, not a paint per se. This argument is not persuasive for the

following reasons. Bonaventura et al clearly states that their mixture is a paint. For example, the title of Example V, which discloses the mixture, is: "Properties of Paints Containing Immobilized Bioactive Materials". In addition, the mixture of Bonaventura et al is encompassed by the genus of "paint", as defined by the specification:

[0309] A paint is a "pigmented liquid, liquefiable or mastic composition designed for application to a substrate in a thin layer which is converted to an opaque solid film after application. Used for protection, decoration or identification, or to serve some functional purpose such as the filling or concealing of surface irregularities, the modification of light and heat radiation characteristics, etc." ["Paint and Coating Testing Manual, Fourteenth Edition of the Gardner-Sward Handbook" (Koleske, J. V. Ed.), p. 696, 1995]. However, as certain coatings disclosed herein are non-film forming coatings, this definition is modified herein to encompass a coating with the same properties of a film forming paint, with the exception that it does not produce a solid film. In particular embodiments, a non-film forming paint possesses a hiding power sufficient to concealing surface feature comparable to an opaque film.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 21-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bonaventura et al, 1999 in view of Di Sioudi et al, 1999 and ExPASy E.C.3.1.8 or Piesecki et al, 1993. The teachings of Bonaventura et al are described above. Bonaventura et al does not teach a paint comprising a structural or sequence analog of their aryldialkylphosphatase. However, it was well known in the art that aryldialkylphosphatases are activated by divalent cations, such as Co^{2+} (Di Sioudi et al, 1999 and ExPASy E.C.3.1.8). Thus, would have been obvious to a person of ordinary skill in the art to use, in the paint of Bonaventura et al, a structural analog of the aryldialkylphosphatase of Bonaventura et al, wherein the structural analog comprises a divalent cation. Motivation to do so is provided by the desire to provide the needed cation to the enzyme.

The expectation of success is high, as it was known that aryldialkylphosphatases are activated by divalent cations, such as Co^{2+} . The making and using of fusion proteins, for example with a tag, was also well known in the art (Piesecki et al, 1993). It would have been obvious to a person of ordinary skill in the art to make a fusion protein comprising the aryldialkylphosphatase of Bonaventura et al and use said fusion protein in the paint of Bonaventura et al. Motivation to do so is provide by the advantage of being able to purify the fusion protein using an affinity agent that binds the tag. As is known in the art, aryldialkylphosphatases require divalent cations, such as Co^{2+} for activity (Di Sioudi et al, 1999 and ExPASy E.C.3.1.8). The expectation of success is high, as methods for making and using fusion proteins comprising enzymes were known in the art. Therefore, Claims 21-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bonaventura et al, 1999 in view of Di Sioudi et al, 1999 and ExPASy E.C.3.1.8 or Piesecki et al, 1993.

Claims 73, 323, and 324 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bonaventura et al, 1999 in view of Sigma, Inc. The teachings of Bonaventura et al are described above. Bonaventura et al further teaches that the aryldialkylphosphatase is active in Glycine/NaOH, pH 9.5 buffer. Bonaventura et al does not teach use of a bicarbonate or dibasic phosphate buffer. It was well known in the art that bicarbonate and dibasic phosphate can buffer at pH 9.5 (Sigma, Inc). It would have been obvious to a person of ordinary skill in the art to use a bicarbonate or dibasic phosphate buffer in the paint of Bonaventura et al. Motivation to do so is provide by the desire to buffer the paint to a pH at which the aryldialkylphosphatase is active. The expectation of success is high, as that the aryldialkylphosphatase is active at pH 9.5 and bicarbonate and dibasic phosphate buffers were known in the art. Therefore, Claims 73, 323, and

324 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bonaventura et al, 1999 in view of Sigma, Inc.

Claims 224-233, 326, and 327 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bonaventura et al, 1999 in view of Pusch et al, 1985. The teachings of Bonaventura et al are described above. Paints comprising pigments are standard in the art and the skilled artisan would believe that, more likely than not, the paint of Bonaventura et al comprised a pigment. However, Bonaventura et al does not specifically teach which pigment is in their paint. Pusch et al teaches paints comprising the infra red transparent pigments chromium oxide and iron oxide (col 7, parg 2). It would have been obvious to a person of ordinary skill in the art to modify the paint of Bonaventura et al to include the chromium oxide or iron oxide pigment of Pusch et al. Motivation to do so is provided by the desire to make and use pigmented paints that are transparent to infra red light. The expectation of success is high, as pigmented paints were well known in the art. Therefore, Claims 224-233 and 326 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bonaventura et al, 1999 in view of Pusch et al, 1985.

Claims 239-242 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Bonaventura et al, 1999 in view of Miller et al, 2005 (priority date 2-JUN-2002). The teachings of Bonaventura et al are described above. Bonaventura et al not teach paint comprising a biocide. Miller et al teaches paint comprising a fungicide (Table 1). It would have been obvious to a person of ordinary skill in the art to incorporate the fungicide of Miller et al into the paint of Bonaventura et al. Motivation to do so derives from the desire to, as taught by Miller et al, inhibit microbial growth in the paint (Table 1). The expectation of success is high, as paints comprising biocides were known in the art (Miller et al). Therefore, Claims 239-242 are

rejected under 35 U.S.C. 103(a) as being unpatentable over the Bonaventura et al, 1999 in view of Miller et al, 2005.

Claim 309 is rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Bonaventura et al, 1999 in view of Ye et al, 1999. The teachings of Bonaventura et al are described above. Bonaventura et al does not teach a container comprising their enzyme in 50% glycerol. Ye et al teach what was well known in the art, that enzymes can be stably stored in 50% glycerol (parg brd pg 19-20). It would have been obvious to a person of ordinary skill in the art to combine the teachings of Bonaventura et al and Ye et al to store the aryldialkylphosphatase enzyme of Bonaventura et al in 50% glycerol prior to mixing with the paint. Motivation to do so derives from the desire to maintain the aryldialkylphosphatase activity after isolation and before making the paint. The expectation of success is high, as storing enzymes in 50% glycerol was well known in the art. Therefore, Claim 309 is rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Bonaventura et al, 1999 in view of Ye et al, 1999.

Claims 321 and 345-347 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bonaventura et al, 1999 in view of Krumhar et al, 1992. The teachings of Bonaventura et al are described above. Bonaventura et al does not teach their paint comprising a colormetric pH indicator. Krumhar et al teach a coating comprising the colormetric pH indicator neutral red (col 5, parg 2). It would have been obvious to a person of ordinary skill in the art to incorporate neutral red into the paint of Bonaventura et al because, as taught by Krumhar et al, neutral red functions as a colormetric pH indicator. Motivation to do so derives from the desire to make and use a paint having sensitivity to environmental pH, which would be advantageous in maintaining activity of the aryldialkylphosphatase. The expectation of success is high, as coatings comprising

colormetric pH indicators were known in the art (Krumhar et al). Therefore, Claims 321 and 345-347 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bonaventura et al, 1999 in view of Krumhar et al, 1992.

Claims 348-350 are rejected under 35 U.S.C. 103(a) as being unpatentable over the Bonaventura et al, 1999 in view of Yafuso et al, 1991. The teachings of Bonaventura et al are described above. Bonaventura et al does not teach their paint comprising a fluorimetric pH indicator. However, fluorimetric pH indicators were well known in the art; see, Yafuso et al for review. Specifically, Yafuso et al teaches a coating comprising HPTS as a fluorimetric pH indicator (col 7, parg 12). It would have been obvious to a person of ordinary skill in the art to incorporate the fluorimetric pH indicators of Yafuso et al into the paint of Bonaventura et al. Motivation to do so derives from the desire to make and use a paint having sensitivity to environmental pH, which would be advantageous in maintaining activity of the arylalkylphosphatase. The expectation of success is high, as fluorimetric pH indicators were well known in the art and Yafuso et al teaches that coatings comprising the fluorimetric indicator HPTS were sensitive to pH (col 7, parg 12). Therefore, Claims 348-350 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bonaventura et al, 1999 in view of Yafuso et al, 1991.

In support of their request that the prior rejections under 35 USC 103(a) be withdrawn, Applicants provide the following arguments, which are relevant to the rejections above. These arguments are not found to be persuasive for the reasons stated after each argument.

(A) In regards to the rejections of claims based on “what is well known in the art”: that OPH activity is regulated by Co²⁺; that fusion proteins of enzymes having activity are useful; that various compounds can be used as pigments; and that isolated enzymes can be stored in 50% glycerol, the Examiner does not provide a cited reference. Hindsight reliance of these teachings

within the specification is being used to provide a motivation to combine these specification teachings with Bonaventura. The Examiner actually cites the specification - the claims - in providing the motivation for the rejection of the very same claims by the statement "that the compounds of claim 226, 230, 233-235, and 326 can be used as pigments (226, 229, 230, 230, 233-235, 326)"! The Examiner has used imperishable hindsight reasoning.

(A) Reply: Reference to the claims was used only to clarify which claims were being referred to, not as a source for support of the rejection. The fact that, it was well known in the art that OPH activity is regulated by Co²⁺; that fusion proteins of enzymes having activity are useful; that various compounds can be used as pigments; and that isolated enzymes can be stored in 50% glycerol, is now provided supporting references.

(B) This reliance on impermissible hindsight is used by the Examiner in citing the references of Krumhar and Pusch as combinable with Bonaventura. The motivation for use of a colormetric indicator (Krumhar) or a camouflage pigment that reduces detection by infrared (Pusch) is provided by the specification, and not these references alone or in combination with Bonaventura. The Examiner has gone so far in using impermissible hindsight in constructing these obviousness rejections as to cite the specification regarding Gillette, rather than the teachings of Gillette itself. Has the Examiner reviewed Gillette for any teaching or motivation to combine with any other reference, or relied upon the specification's disclosure of the claimed invention for the motive to combine? Has the Examiner also relied upon the teachings of the specification in constructing the motivation to combine Krumhar and Pusch with Bonaventura?

(B) Reply: The instant rejections are not based on hindsight reasoning. As explained above, Krumhar et al teach a coating comprising neutral red, which can be used as a colormetric pH indicator. As explained above, Pusch et al teaches paints comprising the pigments chromium

oxide and iron oxide. The reasons the skilled artisan would be motivated to combine Bonaventura et al with Krumhar et al or Pusch et al are explained above.

Although Gillette et al is not used for the rejections herein, the following comments are made. Citing the specification regarding Gillette was used solely to indicate that Gillette need not be provided to Applicants, as they were in possession of the reference. Moreover, rejections based on prior art references cited in the specification or an Information Disclosure Statement are not improper.

Regarding rejections under 35 USC 103(a), the following additional comments are made.

KSR International vs Teleflex Inc. (Federal Register/ Vol. 72, No. 1995, October 10, 2007) takes precedent in the Office's current determination of obviousness under §103(a). Therein, rationales supporting an obviousness rejection are (72 Fed. Reg. 57526; esp pg 57529):

- (a) combining prior art elements according to known methods to yield predictable results,
- (b) simple substitution of one known element for another to obtain predictable results,
- (c) use of a known technique to improve similar devices (methods or products) in the same way,
- (d) applying a known method to a known product or method ready for improvement to yield a predictable result,
- (e) "obvious to try" –choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success,
- (f) known work in one field of endeavor may prompt variations for use in the same or a different field, if the variants would have been predictable, and
- (g) some teaching, suggestion, or motivation in the prior art to lead the skilled artisan to modify or combine prior art teachings.

In the instant case, rationales for supporting the obviousness rejections herein include:

- (a) combining prior art elements according to known methods to yield predictable results,
- (c) use of a known product to improve a similar product in the same way,
- (d) applying a known method (adding a product) to a known product or method ready for improvement to yield a predictable result,
- (e) "obvious to try" –choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success,
- (f) known work in one field of endeavor prompting variations for use in the same or a different field, if the variants would have been predictable.

Allowable Subject Matter

No claims are allowable.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SHERIDAN SWOPE/
Primary Examiner, Art Unit 1652